

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 27 MAR 2006

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## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:  
LAURA PEREIRA  
CATALYST LAW GROUP, APC  
9710 SCRANTON ROAD, SUITE 170  
SAN DIEGO, CA 92121

Date of mailing (day/month/year) 24 MAR 2006

Applicant's or agent's file reference

8028-005-WO

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/33091

International filing date (day/month/year)

07 October 2004 (07.10.2004)

Priority date (day/month/year)

International Patent Classification (IPC) or both national classification and IPC

IPC: C12N 5/06( 2006.01),5/08( 2006.01)

USPC: 435/370

Applicant

MULTICELL TECHNOLOGIES, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

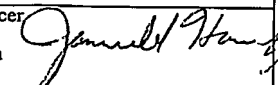
### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

<p>Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201</p>	<p>Date of completion of this opinion 01 March 2006 (01.03.2006)</p>	<p>Authorized officer Vera Afremova  Telephone No. (571) 272-1600</p>
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Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/33091

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing  
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper  
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.  
☐ filed together with the international application in electronic form.  
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

☐ complied with

☒ not complied with for the following reasons:

See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:

☐ all parts.

☒ the parts relating to claims Nos. 1-34

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims 32 and 34 YES

Claims 1-31 and 33 NO

Inventive step (IS)

Claims NONE YES

Claims 1-34 NO

Industrial applicability (IA)

Claims 1-34 YES

Claims NONE NO

2. Citations and explanations:

Please See Continuation Sheet

WRITTEN OPINION OF THE  
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PCT/US04/33091

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-8, 12-21, 23-25, 28 and 30 lack novelty under PCT Article 33(2) as being anticipated by US 5,665,589 (Harris et al).

Claims are directed to a virally immortalized hepatocytes that is derived from normal liver cell, that is nontumorigenic and produces therapeutic plasma proteins (TPPs). Some claims are further drawn to hepatocyte that is derived from human liver, that comprises SV40 Tag DNA, that retains enzymatic activity including cytochrome P450, that produces albumin, transferring, antitrypsin. Some claims are further drawn to indented use of hepatocyte in various assays including drug testing.

US 5,665,589 (Harris et al) discloses a virally immortalized hepatocytes that is derived from human normal liver cell (abstract). The hepatocyte is immortalized with retroviral vector containing SV40 TAG gene and it is nontumorigenic (col. 2, lines 15-25). The hepatocyte produces therapeutic plasma proteins including albumin, transferring and antitrypsin (col. 10, lines 20-27). The hepatocytes retains enzymatic activity including cytochrome P450 (col. 1, line 19). The cited document suggests the use of hepatocyte in various assays including carcinogenesis and drug testing (col. 4, lines 20-25).

Claims 1-31 and 33 lack novelty under PCT Article 33(2) as being anticipated by Mills et al.

Claims are directed to hepatocyte cell line Fa2N-4 that is a virally immortalized hepatocytes, that is derived from normal liver cell, that is nontumorigenic and produces therapeutic plasma proteins (TPPs). Some claims are further drawn to hepatocyte that is derived from human liver, that comprises SV40 Tag DNA, that retains enzymatic activity including cytochrome P450, that produces albumin, transferring, antitrypsin and clotting factors. Some claims are further drawn to indented use of hepatocyte in various assays including drug testing.

Mills et al. discloses hepatocyte cell line Fa2N-4 (see abstract) that is a virally immortalized human hepatocyte cell line. The disclosed cell line is identical to the presently claimed cell line and, thus, considered to have identical abilities as the presently claimed cell lie with regard to enzymatic activity and plasma protein production within the meaning of the claims.

Claims 1-34 lack an inventive step under PCT Article 33(3) as being obvious over Mills et al. and/or US 5,665,589 (Harris et al) in view of US 6,653,105 (Triglia et al).

Claims are directed to hepatocyte cell line that is a virally immortalized hepatocytes, that is derived from normal liver cell, that is nontumorigenic and produces therapeutic plasma proteins (TPPs). Some claims are further drawn to hepatocyte capable to grow in serum-free media. Some claims are further drawn to hepatocyte that is derived from human liver, that comprises SV40 Tag DNA, that retains enzymatic activity including cytochrome P450, that produces albumin, transferring, antitrypsin and clotting factors. Some claims are further drawn to indented use of hepatocyte in various assays including drug testing. Some claims are further drawn to hepatocyte

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